CLAIMS

1. Method for predicting changes of physiological/pathological states in a patient, based on sampling, processing and analyzing a plurality of aggregated noisy biomedical signals, comprising:

a) generating a reference database of raw data streams or features, derived from said raw data streams, representing physiological/pathological states, by aggregating one or more raw data streams, each of which consisting of biomedical signals of a plurality of patients, at least several of which having one or more of said physiological/pathological states, wherein said features are obtained by performing, for each type of biomedical signal, adaptive segmentation of its corresponding raw data streams, and assigning, to each segment, individual attributes being represented by attribute values, thereby obtaining data related to each physiological/pathological states;

b) generating additional data streams using said attributes.

c) Repetition of stages a),b) if needed.

d) determining an attribute domain, in which each segment being represented by a point that corresponds to the attribute values of said segment;

e) for each physiological/pathological state, generating a set of clusters in said attribute domain, each of which consisting of a combination of points determined by their relative location to other points, by assigning a set of property values to each point, each property value corresponding to the degree of association of said point with one of the clusters;

f) associating each point, in time, to a corresponding state;

g) determining the probabilities of transitions between states by obtaining the frequency and the order of appearance of each point, in time;

h) repeating steps d) to f) above while in each time, varying the combination of points included in each cluster according to their most updated property value and by including points derived from said probability until said updated property values remain essentially unchanged, thereby updating each cluster and said probabilities of transitions;

i) generating prior knowledge data, consisting of a plurality of feasible paths between states according to said probabilities of transitions, by associating each feasible path with a corresponding dynamics of transitions between physiological/pathological states;

j) associating at least one updated cluster with a normal/abnormal physiological state of said patient by using former knowledge, regarding normal/abnormal physiological/pathological states;

k) For each patient,

l) aggregating one or more individual data streams or features, derived from said individual data streams, each of which consisting of biomedical signals of said patient, wherein said features are obtained by performing, for each type of biomedical signal, adaptive segmentation of its corresponding raw data streams, and assigning, to each segment, individual attributes being represented by attribute values;

m) Forming additional data streams out of said attributes.

n) Repetition of stages k),l) if needed.

o) assigning each individual attribute to a corresponding state, or to a new state, according to the probability to belong to each existing cluster or to a new cluster associated with said new or existing state and said probabilities of transitions;

p) adaptively updating each existing or new cluster and said probabilities of transitions according to said individual data streams;

q) obtaining a path, being an individual dynamics, between physiological/pathological states according to their order of appearance; and

r) obtaining a prediction of being in, or transitions to, physiological/pathological states in said patient, by comparing said individual dynamics with known dynamics, obtained from prior knowledge.

2. A method according to claim 1, further comprising:

a) Whenever new individual attributes do not belong to an existing cluster, defining one or more new states and transition probabilities between existing states or new states;

b) Obtaining an updated path between said existing states or new states according to their order of appearance;

c) Associating said updated path with an updated individual dynamics of transitions between physiological/pathological states; and

d) Obtaining an updated prediction of physiological/pathological states in said patient, according to said updated individual dynamics and the prior knowledge.

3. A method according to claim 1, further comprising:

Whenever the updated path is a new path reflecting transition between existing states:

a) associating said new path with a new individual dynamics of transitions between physiological/pathological states; and

b) Obtaining a new prediction of physiological/pathological states in said patient, according to said new individual dynamics and the prior knowledge.

4. A method according to claims 2 or 3, further comprising

Updating the reference database, the existing or new clusters, the transition probabilities between existing or new states, and the dynamics of transitions between existing or new physiological/pathological states.

5. A method according to claim 1, wherein the types of biomedical signals are selected from the group:

- ECG signal;
- EEG signal;
- Respiratory signal;
- EOG signals;
- Acoustic signals;
- Oximetry;
- Blood pressure;
- EMG;
- CO2; and
- Body movement/position

6. Method according to claim 1, wherein the features are selected from the groups of:

Spectrum analysis features

- Zero crossing;
- Estimated AR power spectrum;
- Relative peak level of each frequency band;
- Relative energy level of each frequency band;
- Fundamental frequency;
- Number of substantial frequencies; and
- Membership level in each frequency group.

Temporal analysis features

- Maximum and minimum amplitude;
- Maximum and minimum energy;
- Number of substantial peaks;
- Mean, variance and High order statistical moments;
- Duration in seconds and in samples;
- Transient level (derived from the adaptive segmentation algorithm);
- Peak to peak maximum amplitude and duration;
- First derivative (Slope);
- Second derivative;
- Wavelets coefficient calculation;
- PCA coefficient calculation; and
- Matching pursuit based segment decomposition.

Non-linear dynamics features

- The Lempel-Ziv complexity measure;
- Fractal dimension;
- Lyapunov exponent; and
- Density estimation of phase space derived features.

7. A method according to claim 5, wherein the adaptive segmentation of an ECG signal comprises:

a) generating several signals from the raw ECG signal, wherein in each signal a different frequency content being emphasized;

b) summating the corresponding absolute values of said signals;

c) filtering the resulting summation; and

d) employing local maxima detection method, for identifying the R-peaks, P-peaks and T-peaks in said filtered resulting summation, said R, P and T peaks being utilized for characterizing the corresponding heartBeats Under Test (BUTs), said P and T peaks being utilized also for further segmentation of heartbeats.

8. A method according to claim 7, wherein, obtaining features from an ECG signal comprises the steps:

a) detecting 'R-R' time-intervals between each two consecutive R-peaks; and

b) identifying characterizing points 'P', 'Q', 'S' and 'T' of the corresponding BUTs, by utilizing said 'R-R' time-intervals, at least some of said points being utilized for obtaining features related thereto.

9. A method according to claim 8, wherein identifying the R-peaks in the ECG signal is carried out by utilizing the Wavelet Transform Process with several scales associated with said R-peaks.

10. A method according to claim 8, wherein the features that are obtained from the ECG signal are:

a) The general shape of PQRST complex, which is obtained by utilizing pattern recognition technique, the Wavelets algorithm, and PCA;

b) Intervals, which relate to consecutive P, Q, R, S and T points of heartbeats;

c) Interval differences, which relate to differences of the intervals of b);

d) Interval ratios, which relate to ration between intervals of b);

e) Differentials of 'nth" order (n=1,2,..) of consecutive intervals; and

f) Absolute values of the differentials mentioned in e).

11. A method according to claim 10, wherein the features of e) and f) are obtained with respect to:

(1) Single heartbeats; or
(2) Heartbeat ensemble averages, variance and RMS of differences; or
(3) Heartbeat ensemble distributions.

12. A method according to claim 1, wherein the adaptive segmentation of an all physiological and derived signals comprises utilization of a first and a second time-windows, the time-width and relative location being varied until a decision, regarding the optimized location of the boundaries of each EEG segment, is determined, based on the comparison between the statistical properties of a first signal portion contained in the first time-window to the statistical properties of a second signal portion contained in the second time-window.

13. A method according to claim 12, wherein the comparison is implemented using the GLRT and KLD measures.

14. A method according to claim 5, wherein the adaptive segmentation of the Respiratory signal comprises:

a) Detection and Smoothing of the envelope of a corresponding chest and abdomen effort signals, air pressure flow signal, and thermistor flow signal;
b) Peak Detection and Maximum Setting of the envelope signal; and
c) Identifying two consecutive global maxima points, said points defining the temporal boundaries of a corresponding segment of said envelope.

15. A method according to claim 5, wherein features that are obtained from acoustic signals are related to spectral features and peak velocities, which are obtained from beat-induced intra-cardiac sounds and Doppler-shift effect of intra-vascular (coronary) blood flow, respectively.

16. A method according to claim 1, wherein the set of clusters is generated by employing un-supervised fuzzy clustering algorithm on the points residing within the corresponding attribute domain.

17. A method according to claim 1, wherein the classification of the extracted features is implemented by utilization of one or more HMM models, each of which could be characterized by having different number of states and free parameters.

18. A method according to claim 17, wherein different HMM models are trained to characterize different global physiological/pathological behavior, which may be associated with specific group of population, sleep stage or any health condition.

19. A method according to claim 17 or 18, wherein the prediction process utilizes one or more HMM models and one or more sets of fuzzy logic rules that are employed on the factors/features: (1) pathological heartbeats, (2) patient's weight or height or general health/condition, (3) blood pressure, (4) sleep stage, and (5) oxygen in the blood, in order to obtain a more reliable prediction result.

20. A method according to claims 17 to 19, wherein different mixtures of HMM models are utilized, each of which is optimal with respect to different monitoring stage, time epoch and biomedical signal.

21. A method according to claim 1, further comprising:

Generating, in real-time, alert indications representing abnormal physiological events; and

a) Automatically transmitting said indications to a physician over a data network, for determining/providing the required medical treatment.

22. A method according to claim 1, further comprising dynamically controlling the operation of a medical apparatus used for providing medical treatment to a patient being monitored, in response to identified pre-pathological state(s) in said patient, for preventing the occurrence of the pathological state(s).

23. A method according to claim 22, wherein the medical apparatus is an apparatus that is selected from the following group of apparatuses, or an apparatus operable using combined principles of several of these apparatuses:

- Controllable drug dosage devices;
- Controllable gas/air delivery devices;
- Continuous Positive Airway Pressure (CPAP);
- Bi-level positive airway pressure (BPAP);
- Implantable/non-implantable Respiratory Stimulator;
- Implantable/non-implantable Brain/Nerve Stimulator/Pacers;
- Implantable/non-implantable cardiac defibrillators (ICD)/cardiac pacers/Cardiac Resynchronization Therapy (CRT).

24. System for predicting changes of physiological/pathological states in a patient, based on sampling, processing and analyzing a plurality of aggregated noisy biomedical signals, comprising:

a) Data acquisition means for collecting biomedical signals of one or more patients;

b) A database of data streams or features, derived from said data streams, representing physiological/pathological states, said database aggregates one or more raw data streams, each of which consisting of said biomedical signals of a plurality of patients, at least several of which having one or more of said physiological/pathological states, said database being capable of storing data streams or features which are used as reference data streams or features for characterizing further individual patients and for storing data streams or features of individual patients;

c) Processing means for obtaining said features by performing, for each type of biomedical signal, adaptive segmentation of its corresponding raw data streams, and assigning, to each segment, individual attributes being represented by attribute values, and for obtaining data related to each physiological/pathological states; and

d) Additional processing means for determining an attribute domain, in which each segment being represented by a point that corresponds to the attribute values of said segment; for generating a set of clusters in said attribute domain for each physiological/pathological state wherein each of which consisting of a combination of points determined by their relative location to other points, for assigning a set of property values to each point, wherein each property value corresponding to the degree of association of said point with one of the clusters; for associating each point, in time, to a corresponding state; for determining the probabilities of transitions between states by obtaining the frequency and the order of appearance of each point, in time; for varying the combination of points included in each cluster according to their most updated property value and for including points derived from said probability until said updated property values remain essentially unchanged, so as to update each cluster and said probabilities of transitions; for generating prior knowledge data, consisting of a plurality of feasible paths between states according to said probabilities of transitions, by , and for associating each feasible path with a corresponding dynamics of transitions between physiological/pathological states; for associating at least one updated cluster with a normal/abnormal physiological state of said patient by using former knowledge, regarding normal/abnormal physiological/pathological states; for performing, for each type of biomedical signal, adaptive segmentation of its corresponding raw data streams, and for assigning, to each segment, individual attributes being represented by attribute values, for assigning each individual attribute to a corresponding state, or to a new state, according to the probability to belong to each existing cluster or to a new cluster associated with said new or existing state and said probabilities of transitions ; for adaptively updating each existing or new cluster and said probabilities of transitions according to said individual data streams; for obtaining a path, being an individual dynamics, between physiological/pathological states according to their order of appearance, and associating said most feasible path with an individual dynamics of transitions between physiological/pathological states; and for obtaining a prediction of being in, or transitions to, physiological/pathological states in said patient, by comparing said individual dynamics with known dynamics, obtained from prior knowledge.

25. System according to claim 24, further comprising processing means for defining one or more new states and transition probabilities between existing states or new states whenever new individual attributes do not belong to an existing cluster; obtaining an updated path between said existing states or new states according to their order of appearance; for associating said updated path with an updated individual dynamics of transitions between physiological/pathological states; and for obtaining an updated prediction of physiological/pathological states in said patient, according to said updated individual dynamics and the prior knowledge.

26. System according to claim 24, further comprising processing means for associating the new path with a new individual dynamics of transitions between physiological/pathological states; and for obtaining a new prediction of physiological/pathological states in said patient, according to said new individual dynamics and the prior knowledge, whenever the updated path is a new path reflecting transition between existing states.

27. System according to claims 25 or 26, further comprising processing means for updating the reference database, the existing or new clusters, the transition probabilities between existing or new states, and the dynamics of transitions between existing or new physiological/pathological states.

28. System according to claim 24, in which the types of biomedical signals are selected from the group:

- ECG signal;
- EEG signal;
- Respiratory signal;
- EOG signals;
- Acoustic signals;
- Oximetry; and
- Blood pressure;
- EMG;
- CO2; and
- Body movement/position

29. System according to claim 24, in which the features are selected from the groups of:

Spectrum analysis features

- o Zero crossing;
- o Estimated AR power spectrum;
- o Relative peak level of each frequency band;
- o Relative energy level of each frequency band;
- o Fundamental frequency;
- o Number of substantial frequencies; and
- o Membership level in each frequency group.

Temporal analysis features

- o Maximum and minimum amplitude;
- o Maximum and minimum energy;
- o Number of substantial peaks;
- o Mean, variance and skewness;

- Duration in seconds and in samples;
- Transient level (derived from the adaptive segmentation algorithm);
- Peak to peak maximum amplitude and duration;
- First derivative (Slope);
- Second derivative;
- Wavelets coefficient calculation;
- PCA coefficient calculation; and
- Matching pursuit based segment decomposition.

Non-linear dynamics features

- The Lempel-Ziv complexity measure;
- Fractal dimension;
- Lyapunov exponent; and
- Density estimation of phase space derived features.

30. System according to claim 28, in which the adaptive segmentation of an ECG signal comprises:

a) Circuitry for generating several signals from the raw ECG signal, wherein in each signal a different frequency content being emphasized;
b) Circuitry for summating the corresponding absolute values of said signals;
c) Circuitry for filtering the resulting summation; and
d) Processing means for identifying the R-peaks, P-peaks and T-peaks in said filtered resulting summation, said R, P and T peaks being utilized for characterizing the corresponding heartBeats Under Test (BUTs), said P and T peaks being utilized also for further segmentation of heartbeats, by employing local maxima detection method.

31. System according to claim 30, comprising processing means for obtaining features from an ECG signal, by detecting ‘R-R’ time-intervals between each two consecutive R-peaks; and identifying characterizing points ‘P’, ‘Q’, ‘S’ and ‘T’ of the corresponding BUTs, by utilizing said ‘R-R’ time-intervals, at least some of said points being utilized for obtaining features related thereto.

32. System according to claim 31, comprising processing means for identifying the R-peaks in the ECG signal by utilizing the Wavelet Transform Process with several scales associated with said R-peaks.

33. System according to claim 31, in which the features that are obtained from the ECG signal are:

a) The general shape of PQRST complex, which is obtained by utilizing pattern recognition technique, the Wavelets algorithm, and PCA;
b) Intervals, which relate to consecutive P, Q, R, S and T points of heartbeats;
c) Interval differences, which relate to differences of the intervals of b);
d) Interval ratios, which relate to ration between intervals of b);
e) Differentials of 'nth" order (n=1,2,..) of consecutive intervals; and
f) Absolute values of the differentials mentioned in e).

34. System according to claim 33, in which the Differentials of 'nth" order (n=1,2,..) of consecutive intervals and the absolute values of said differentials are obtained with respect to:

a) Single heartbeats; or
b) Heartbeat ensemble averages, variance and RMS of differences; or
c) Heartbeat ensemble distributions.

35. System according to claim 28, in which the adaptive segmentation of an EEG signals comprises utilization of a first and a second time-windows, the time-width and relative location being varied until a decision, regarding the optimized location of the boundaries of each EEG segment, is determined, based on the comparison between the statistical properties of a first EEG signal portion contained in the first time-window to the statistical properties of a second EEG signal portion contained in the second time-window.

36. System according to claim 35, in which the comparison is implemented using the GLRT and KLD measures.

37. System according to claim 28, comprising processing means for adaptive segmentation of the Respiratory signal by detection and Smoothing of the envelope of a corresponding chest effort, abdomen effort signals, air pressure flow signal, and thermistor flow signal; Peak Detection and Maximum Setting of the envelope signal; and identifying two consecutive global maxima points, said points defining the temporal boundaries of a corresponding segment of said envelope.

38. System according to claim 28, in which features that are obtained from acoustic signals are related to spectral features and peak velocities, which are obtained from beat-induced intra-cardiac sounds and Doppler-shift effect of intra-vascular (coronary) blood flow, respectively.

39. System according to claim 24, in which the set of clusters is generated by employing un-supervised fuzzy clustering algorithm on the points residing within the corresponding attribute domain.

40. System according to claim 24, in which the classification of the extracted features is implemented by utilization of one or more HMM models, each of which could be characterized by having different number of states and free parameters.

41. System according to claim 40, in which different HMM models are trained to characterize different global physiological/pathological behavior, which may be associated with specific group of population, sleep stage or any health condition.

42. System according to claim 40 or 41, in which the prediction process utilizes one or more HMM models and one or more sets of fuzzy logic rules that are employed on the factors/features: (1) pathological heartbeats, (2) patient's weight or height or general

health/condition, (3) blood pressure, (4) sleep stage, and (5) oxygen in the blood, in order to obtain a more reliable prediction result.

43. System according to claims 40 to 42, in which different mixtures of HMM models are utilized, each of which is optimal with respect to different monitoring stage, time epoch and biomedical signal.

44. System according to claim 24, further comprising processing means for generating, in real-time, alert indications representing abnormal physiological events; and for automatically transmitting said indications to a physician over a data network, for determining/providing the required medical treatment.

45. System according to claim 24, further comprising processing means for dynamically controlling the operation of a medical apparatus used for providing medical treatment to a patient being monitored, in response to identified pre-pathological state(s) in said patient, for preventing the occurrence of the pathological state(s).

46. System according to claim 45, in which the medical apparatus is an apparatus that is selected from the following group of apparatuses, or an apparatus operable using combined principles of several of these apparatuses:
- Controllable drug dosage devices;
- Controllable gas/air delivery devices;
- Continuous Positive Airway Pressure (CPAP);
- Bi-level positive airway pressure (BPAP);
- Implantable/non-implantable Respiratory Stimulator;
- Implantable/non-implantable Brain/Nerve Stimulator/Pacers;
- Implantable/non-implantable cardiac defibrillators (ICD)/cardiac pacers/Cardiac Resynchronization Therapy (CRT).